Ancient–Modern Concordance in Ayurvedic Plants: Some Examples

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Ayurveda is the ancient (before 2500 B.C.) Indian system of health care and longevity. It involves a holistic view of man, his health, and illness. Ayurvedic treatment of a disease consists of salubrious use of drugs, diets, and certain practices. Medicinal preparations are invariably complex mixtures, based mostly on plant products. Around 1,250 plants are currently used in various Ayurvedic preparations. Many Indian medicinal plants have come under scientific scrutiny since the middle of the nineteenth century, although in a sporadic fashion. The first significant contribution from Ayurvedic materia medica came with the isolation of the hypertensive alkaloid from the sarpagandha plant (*Rauwolfia serpentina*), valued in Ayurveda for the treatment of hypertension, insomnia, and insanity. This was the first important ancient–modern concordance in Ayurvedic plants. With the gradual coming of age of chemistry and biology, disciplines central to the study of biologic activities of natural products, many Ayurvedic plants have been reinvestigated. Our work on *Commiphora wightti* gum-resin, valued in Ayurveda for correcting lipid disorders, has been described in some detail; based on these investigations, a modern antihyperlipoproteinemic drug is on the market in India and some other countries. There has also been concordance for a few other Ayurvedic crude drugs such as *Asparagus racemosus, Cedrus deodara,* and *Psoralea corylifolia. Key words*: γ-aminobutyric acid, antihyperlipoproteinemic drug, *Asparagus racemosus,* Ayurveda, bakuchiol, *Cedrus deodara, Commiphora wightti,* GABA, guggulsterones, himachalol, *Psoralea corylifolia,* reserpine, *Rauwolfia serpentina. Environ Health Perspect* 107:783–789 (1999). [Online 25 August 1999]
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In the early development of modern medicine, biologically active compounds from higher plants have played a vital role in providing medicines to combat pain and diseases. For example, in *The British Pharmacopoeia* of 1932 (*1*), over 70% of organic monographs were on plant-derived products. However, with the advent of synthetic medicinals, and subsequently of antibiotics, the role of plant-derived therapeutic agents significantly declined (mostly) in the economically developed nations. Thus, in the 1980 edition of the *The British Pharmacopoeia* (*2*), the share of plant-based monographs fell to approximately 20%. In terms of new chemical entities introduced as medicinal agents over the past several decades, the share of plant-based drugs has been no more than 2% (*3*). However, plant-derived medicinals continue to occupy an important niche in the treatment of diseases worldwide. Thus, most of the recently introduced plant-based drugs have been innovative in character and represent outstanding contributions to therapeutics. These drugs include several anticancer agents such as podophyllotoxin, paclitaxel, camptothecin, or compounds based on these as lead structures; each of these classes of compounds exhibit their anticancer activity by distinct mechanisms (*3*). It has been estimated that in the United States, 25% of all prescriptions dispensed from community pharmacies during the period 1959–1980 contained plant extracts or active principles derived therefrom (*4*). Even now, 75–80% of the world population depends on crude plant drug preparations to treat their health problems, although this may be mostly because of economic considerations.

In the last two decades, there has been a new trend in the preparation and marketing of drugs based on medicinal plants (*3,5–8*). These preparations, labeled herbal drugs or phytomedicines, are single plant extracts or fractions thereof and are distinct from the pure chemical entities of molecular drugs (*3*). These new plant-derived products are carefully standardized, and their efficacy and safety for a specific application have been demonstrated. The present global market for these products has been estimated to be approximately $20 billion U.S. and is growing at the rate of 15–20% annually (*3*).

Thus, plant-based therapeutic agents continue to have scientific, social, and commercial significance and appear to be gathering a momentum in health-relevant areas.

A study of the process by which the traditional or more recent plant-based molecular drugs or the new breed of herbal drugs came to be used in present-day medicine reveals that, in over 70% of the cases, the starting point has been some reference to the use of that plant as an indigenous cure in a folklore or traditional system of medicine of one culture or another. Some examples are codeine, ephedrine, quinine, and emetine among the traditional molecular drugs; reserpine, artemisinin, and podophyllotoxin (lead structure) from the period after the traditional molecular drug era; and garlic, ginseng and St. John's wort of the currently popular herbal drugs. Thus, this paper highlights the modern drug discovery potential of the plants described in various traditional systems of medicine or in the folklore of various countries, which has been previously emphasized (*3,9–12*). It is with this background that I would like to discuss the potential of and opportunity in Ayurvedic materia medica. However, it seems appropriate to briefly describe Ayurveda for those not familiar with this Indian heritage.

Ayurveda

The origin of Ayurveda has been lost in prehistoric antiquity, but its characteristic concepts appear to have matured between 2500 and 500 B.C. in India. The word "Ayurveda" is derived from "ayus (r)," meaning life, and "veda," meaning knowledge; thus, Ayurveda literally means "science of life." It is the ancient Indian system of health care and longevity. Ayurveda takes a holistic view of man, his health, and illness. It aims at positive health, which has been defined as a well-balanced metabolism coupled with a healthy state of being. Disease, according to Ayurveda, can arise from the body and/or the mind because of external factors or intrinsic causes. Ayurvedic treatment is aimed at the patient as an organic whole,

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and treatment consists of salubrious use of drugs, diets, and certain practices (*13*).

Ayurveda has a vast literature in Sanskrit and various Indian languages, covering various aspects of diseases, therapeutics, and pharmacy. It has evolved its own theoretical base, which is difficult to comprehend in terms of modern scientific concepts, at least at present. However, here we are concerned only with the exploration of its materia medica.

Pharmaceutics occupies an important place in Ayurveda. Medicinal preparations are complex mixtures including plant- and animal-derived products, minerals, and metals. Plants form a dominant part of Ayurvedic pharmacopoeia. The earliest references to such plants are found in the *Rig Veda* and the *Atharva Veda*, dating back to the second millennium B.C. The *Charaka Samhita* (~ 900 B.C.) (*14,15*) is the first recorded treatise fully devoted to the concepts and practice of Ayurveda; its primary focus was therapeutics. This work listed 341 plants and plant products for use in medicine. The next landmark in Ayurvedic literature was the *Sushruta Samhita* (~ 600 B.C.) (*16,17*), which has special emphasis on surgery. It described 395 medicinal plants, 57 drugs of animal origin, and 64 minerals and metals as therapeutic agents. Sushruta, the father of surgery, lived and practiced surgery in Varanasi, India, approximately 2,500 years ago. Another important authority in Ayurveda was Vagbhatta of Sind, in present day Pakistan, who practiced around the seventh century A.D. His work *Ashtanga Hridaya* is considered unrivaled for the principles and practice of medicine (*13,18*). The *Madhava Nidana* (~ 800–900 A.D.) was the next important milestone; it is the most famous Ayurvedic work on the diagnosis of diseases (*16*). The last celebrated writer on Hindu medicine was Bhava Mishra of Magadha, whose treatise *Bhava Prakasha*, written around 1550, is held in high esteem by modern Ayurvedic practitioners for its descriptions of approximately 470 medicinal plants (*19*). Other than these monumental treatises, many (> 70) Nighantu Granthas (pharmacy lexicons) were written, mostly between the seventh and sixteenth centuries (*13,16*). *Raj Nighantu* by Narhari Pandita and *Madanpala Nighantu* by Madanpala are considered masterpieces on medicinal plants (*12*).

Table 1. Classification of plant drugs according to *Charaka Samahita* (*21*).[a]

No.	Sanskrit name	Use
1	Jivaniya	Promoting longevity
3	Lekhaniya	Antiobesity
6	Dipaniya	Promotor of digestion
7	Balya	Promoting strength
8	Varnya	Promoting complexion
15	Krmighna	Anthelmintic
17	Stanyajanana	Galactagogue
23	Vamanopaga	Emetic
24	Virechanopaga	Purgative
35	Mutravirechaniya	Diuretic
36	Kasahara	Antitussive
38	Svayathuhara	Antiinflammatory
39	Jvarahara	Febrifuge
47	Vedanasthapana	Analgesic
50	Vayahsthapana	Antiaging

[a]Listing is only partial.

All ancient texts on Ayurveda divide medical knowledge into eight branches (Ashtanga), and this is no different from the contemporary approach. Also, Ayurvedic descriptions of diseases are much like the modern delineation (*20*). Plant-derived drugs have been categorized according to their pharmacologic/therapeutic action. For example, in the *Charaka Samhita*, drugs were classified into 50 groups (Table 1) (*21*).

Ayurveda, in its prime, was a cogent, scientifically organized discipline. Ayurvedic texts were much respected in neighboring countries, as evidenced from their translation into Greek (300 B.C.), Tibetan and Chinese (300 A.D.), Persian and Arabic (700 A.D.), and several languages of other Asian people (*22,23*). Currently, Ayurveda is widely practiced in the Hindustan peninsula (India and the neighboring countries) and, in recent years, has attracted much attention in economically developed countries such as those in Europe and in the United States and Japan (*24*).

Ayurvedic Drugs

There are approximately 1,250 Indian medicinal plants (*25*) that are used in formulating therapeutic preparations according to Ayurvedic or other traditions. Several of these plants came under the contemporary (modern) scientific scrutiny since the middle of the nineteenth century. A fairly comprehensive account of early research covering the period up to the early 1930s was incorporated into book form (*26*), and this book was revised and updated in 1958 (*27*). In 1961, the Central Council of Ayurvedic Research, Government of India, arranged a conference of reputed Ayurvedic physicians to prepare a list of the most useful Ayurvedic plants. Thus, a list of 190 single plant drugs emerged. This was followed-up by the formulation of a composite drug research scheme by the Ministry of Health, in collaboration with the Indian Council of Medical Research and the Council of Scientific and Industrial Research. The aim of this scheme was to include prominent scientists of the country involved in both Ayurvedic and modern clinical practice, pharmacology, pharmacognosy, and chemistry in an effort to evaluate the classical claims in terms of contemporary scientific knowledge. Results of these investigations have been summarized (*28,29*).

Two other major screening programs were launched around 1964, one at the Central Drug Research Institute (CDRI), Lucknow, India (*30*), and the other at Ciba-Geigy Research Centre, Mumbai, India (*31*). Both of these programs covered the Indian flora in general, without reference to any use of these plants in Ayurveda or in any Indian folklore. The outcome of the Ciba-Geigy program has not been made public. On the other hand, the CDRI effort, spanning a period of 20 years, covered over 2,500 plants that were screened for a variety of biologic activities. Interesting leads were apparently obtained, and these results have been summarized (*32*).

Indian medicinal plants have been studied in various universities and research institutes; this work is still in progress, with results being reported in professional journals.

Table 2. Some Ayurvedic crude drugs that have received pharmacologic and clinical support for their therapeutic claims.

Plant		Active component	Type of activity (references)
Botanical name	Sanskrit name		
Acorus calamus	Vacha	Unknown	Tranquilizer (*28*)
Adhatoda zeylanica	Vasa	Vasicine	Bronchodilator, oxytocic (*35*)
Aloe vera	Kumaari	Unknown	Antiinflammatory (*36–38*)
Andrographis paniculata	Bhuinimba	Andrographolide	Hepatoprotector (*39,40*)
Asparagus racemosus	Shatavari	Shatavarn-I	Antiabortifacient (*41–43*)
Azadirachta indica	Nimb	Gedunin	Antimalarial (*44,45*)
Bacopa monneri	Brahmi	Baccosides	Improves memory (*46*)
Boerhaavia diffusa	Punarnava	Unknown	Diuretic, antiinflammatory (*28*)
Boswellia serrata	Sallakee	Boswellic acids	Antiarthritic (*47,48*)
Butea frondosa	Palasha	Palasonin	Anthelmintic (*28,49*)
Cedrus deodara	Devadaru	Himachalols	Spasmolytic (*50,51*)
Centella asiatica	Mandookpaarni	Asiaticosides	Skin diseases, psychotropic (*28,52*)
Commiphora wightti	Guggulu	Guggulsterones	Hypolipidemic (*53–55*)
Curcuma longa	Haridra	Curcumin	Antiinflammatory (*48,56*)
Holarrhena antidysenterica	Kutaja	Conessine	Antidysenteric (*29*)
Phyllanthus niruri	Bhoomyaamalakee	Unknown	Hepatoprotector (*57,58*)
Picrorrhiza kurroa	Katukaa	Picroside, kutcoside	Hepatoprotector (*59–62*)
Psoralea corylifolia	Bakuchi	Psoralen, bakuchiol	Antileucoderma, antibacterial (*29*)
Rauwolfia serpentina	Sarpagandha	Reserpine	Tranquilizer (*63,64*)
Swertia chirata	Kairata	Unknown	Hepatoprotector (*65,66*)

Two publications (*33,34*) have attempted to cover these findings.

In a significant number of cases, current data from these and other studies corroborate the main claims of these plants according to traditional use. Some examples are shown in Table 2 (*35–66*). This concordance is meaningful; to emphasize its scientific, commercial, and social potential, I would like to elaborate on some of these examples.

Psoralea corylifolia ***(bakuchi).*** This is an erect annual found almost throughout India. Its seed powder is valued in Ayurveda for the treatment of vitiligo, psoriasis, and inflammatory diseases of the skin (*67*). Chemical and pharmacologic investigations (*29,68,69*) led to the isolation of the active principle, psoralen (Figure 1), in the mid-1930s; psoralen has been shown to stimulate the formation of melanin (*70*). Psoralen is used therapeutically for the treatment of leucoderma. More recent investigations have led to the isolation of the meroterpene bakuchiol (Figure 1) (*71–73*) and other related compounds (*74*). Bakuchiol has been shown to posses potent antibacterial activity (*29*) and is useful for the treatment of psoriasis (*75*). Recently, bakuchiol has been shown to be a DNA polymerase inhibibitor (*76*).

Rauwolfia serpentina ***(sarpagandha).*** This is a famous Ayurvedic plant because it represents the earliest (~ 1950) contribution of Ayurveda to modern drug development. *Rauwolfia serpentina* received international attention and rekindled the interest of researchers in exploring higher plants for innovative leads. Roots of this plant are valued in Ayurveda for the treatment of hypertension, insomnia, and insanity (*63*); in Hindi speaking areas, this plant is called "pagle ki booti" (plant for the insane). Significant pharmacologic, clinical, and chemical work on the plant carried out in India attracted the attention of the CIBA group (Basel, Switzerland), who finally succeeded (in 1952) in isolating the sedative principle, reserpine, a minor alkaloidal constituent. Reserpine was introduced in the market in 1953 and was heralded as a revolutionary event in the treatment of hypertension, as it had the twin effect of lowering high blood pressure and acting as a tranquillizer (*64*).

Asparagus racemosus ***(shatavari).*** Roots of *Asparagus racemosus* are reputed in Ayurveda as galactagogue, and preparations based on this drug (e.g., Shatavari sidh ghrit) are often recommended in cases of threatened abortion (*28,77*). This plant contains several glycosides, and one of these, shatavaran-I (Figure 1) (*41,42*), has been shown to block oxytocin-induced contractions in rat, guinea pig, and rabbit uteri *in vivo* and *in situ* (*78*). Galactagogue activity has also received some experimental support (*43*).

Cedrus deodara ***(devadaru).*** Wood of the Himalayan cedar has several medicinal attributes, and preparations based on this plant are used to treat cough, bronchitis, and skin diseases, among others (*79*). An oil obtained from the wood is used in villages for treating insect infestations on animals; there is sufficient experimental support for this (*80*). The essential oil of the wood has been thoroughly examined chemically (*81–83*). Himachalol (Figure 1), one of the constituents of the essential oil, has been shown to possess potent spasmolytic activity (*50,51*). Activity-guided fractionation led to the identification of himachalenes (Figure 1) as the antimange compounds. A commercial preparation (Flematic) based on this finding is being marketed (*84*) in India as a broad spectrum agent against various types of ectoparasites that commonly affect animals.

Commiphora wightti ***(guggulu).*** *Commiphora wightti* is another significant contribution of Ayurveda to modern medicine. *Commiphora wightti* is a small tree belonging to the family Burseraceae; when injured, the plant exudes a yellowish gum resin that soon solidifies to an agglomerate of tears or stalactitic pieces with balsamic odor. This gum resin ("guggulu" in Sanskrit) is renowned in Ayurveda for the treatment of inflammatory disorders, rheumatoid arthritis, lipid disorders, obesity, skin diseases, and other ailments (*85*). Some of these claims appeared to be supported by the results of pharmacologic screening (*53,86–89*) carried out during 1960–1969 on the crude drug. In *Sushruta Samhita,* the description of medoroga (obesity and associated lipid disorders) is quite reminiscent of the modern concepts of pathogenesis of atherosclerosis (Figure 2) (*90*), and guggulu was recommended for treatment. In 1969, few drugs with useful hypolipidemic activity were on the market.

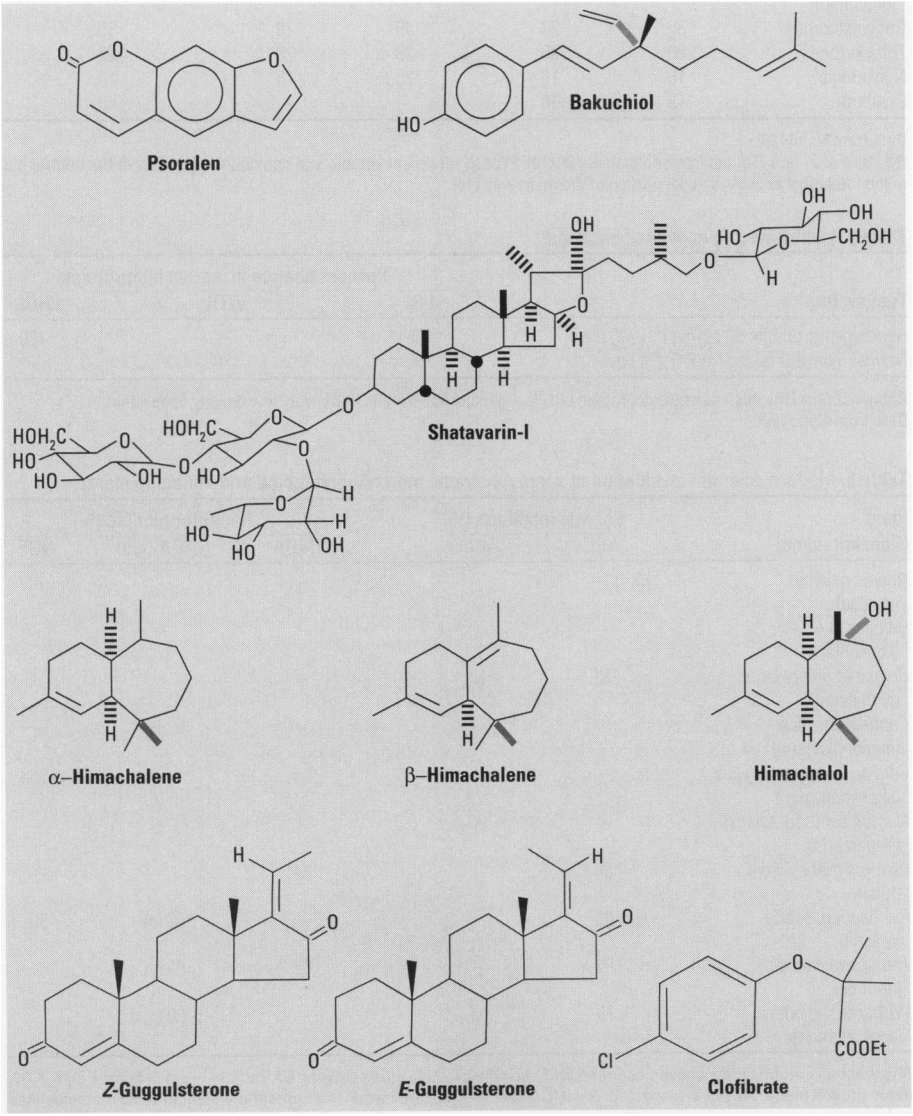

Figure 1. Diagrams of various chemical compounds present in some useful Ayurvedic plants.

Bioassay-guided separation eventually led, in 1971, to the isolation and characterisation of two antihyperlipoproteinemic compounds, *Z*-guggulsterone and *E*-guggulsterone (Figure 1) (*54,55*). Both compounds have similar activity comparable (Table 3) to that of clofibrate (Figure 1), a synthetic hypolipemic drug that became available on the market in 1967.

Guggulu gum resin essentially consists of an ethyl acetate-soluble fraction (~ 45%) and an insoluble carbohydrate gum (~ 55%). The latter is toxic to rats and is devoid of any hypolipemic activity. The desired biologic activity lies entirely in the ethyl acetate-soluble fraction. This fraction has been extensively chemically examined (*54, 91–97*) and consists of diterpenoids, triterpenoids, steroids, lignans, fatty tetrol esters, etc. A review of this work has been published (*98*). Approximately 4% of the active guggulsterones are present in this fraction. However a comparison (Table 3) of the activity of this fraction with that of pure guggulsterones showed a vastly disproportionate activity for the total extract, possibly due to synergistic or additive activity of some of the components of the mixture (*12*). In view of this, further development of the product (collecting pharmacologic, biochemical, toxicologic, teratogenic, mutagenic, and clinical data) was carried out on a standardized ethyl acetate extract, code-named gugulipid, containing at least 4% guggulsterones. Gugulipid exhibits a dose-dependent lowering of serum cholesterol and triglycerides in normal and hyperlipidemic rats, rabbits, and monkeys. A study of the lipoprotein profile in rabbits (Table 4) showed a significant enhancement in the level of the desired high-density lipoproteins and reduction in the unwanted low-density lipids (*99*). Gugulipid also caused regression of atheromatous lesions induced in rabbits by a fat-rich diet. Gugulipid has a multifocal action: it inhibits cholesterol biosynthesis, mobilizes fat from tissues, and increases secretion of bile acids (*100–102*). Although guggulsterones are pregnane derivatives, they are completely devoid of any estrogenic, antiestrogenic, or progestational activity. Gugulipid was cleared for registration in India in 1986, and the drug has been manufactured and marketed in India since 1987. Gugulipid is now being sold in the international market.

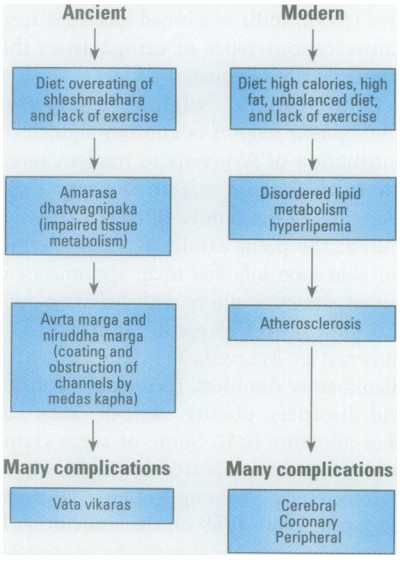

Figure 2. Analogy drawn between the modern concept of pathogenesis of atherosclerosis and the ancient concept of the pathogenesis of obesity and associated lipid disorders. Definitions: shleshmalahara, rich food (fats, proteins); vata vikaras, diseases of the nervous system.

The discovery of antihyperlipoproteinemic guggulsterones in the guggulu resin was an event of considerable interest because these compounds represent a new structural type in hypolipidaemic agents (*103*). Consequently, a number of pregnane derivatives were synthesized and evaluated for their hypolipemic activity. One of these (code no. 81/574) was found to be at least as active as guggulsterones and is currently undergoing clinical trials (*99*).

Additional Concordance

In recent years we have studied several groups of Ayurvedic plants by modern *in vitro* methods, in colloboration with various groups. A brief account of these investigations follows.

Table 3. A comparison of cholesterol-lowering activity of guggulsterones, clofibrate, and some guggulu fractions in rats.

Product (100 mg/kg, oral for 30 days)	Percent lowering of serum lipids				Percent inhibition of cholesterol biosynthesis in rat liver homogenate
	Normal rats		Rats fed high fat		
	Cholesterol	Triglycerides	Cholesterol	Triglycerides	
Ethyl acetate soluble (gugulipid)	34	24	46	24	30
Guggulsterones[a]	35	28	48	29	35
Total ketones[b]	30	26	29	20	22
Nonketonic[b]	15	16	25	15	10
Clofibrate	43	30	–	–	40

Data from Nand (*99*).
[a]Mixture of *Z*- and *E*-guggulsterone isomers (80:20). [b]These represent ketonic and nonketonic fractions of the neutral cut of the total ethyl acetate-soluble portion of the gum resin (*15*).

Table 4. Lipid-lowering activity of gugulipid

Test system	Percent change in serum lipoproteins		
	LDL	VLDL	HDL
Hyperlipemic rabbits 50 mg/kg P.O./90 days	-25	-27	+29
Normal monkeys 60 mg/kg P.O./90 days	-50	-30	–

Abbreviations: HDL, high density lipoprotein; LDL, low density lipoprotein; VLDL, very low density lipoprotein.
Data from Nand (*99*).

Table 5. Modern scientific evaluation of some Ayurvedic memory-enhancing and antiaging plants.

Plant (Sanskrit name)	Enzyme inhibition (%)		Receptor binding (%)		
	ACE	AChE	NMDA	GABA (A/B)	NGF
Acorus calamus (vaccha)	–	–	–	–	–
Benincasa hispida (kooshmand)	–	–	–	–	–
Celastrus paniculatus (jyotishmati)	NI	NI	–	–	–
Centella asiatica (mandookpaarni)	–	–	–	82 (B)	–
Convolvulus microphyllus (shankhapushpi)	–	–	55	–	High
Nardostachys jatamansi (jataamansi)	–	90	–	–	–
Ocimum gratissimum (tulsi)	68	–	NI		
Pluchea lanceolata (raasna)	60	–	–	99 (B)	50
Terminalia chebula (haritaki)	82	–	53	53 (B)	–
Withania somnifera (ashwagandha)	NI	NI	–	> 80 (A,B)	–

Abbreviations: AChE, acetylcholine esterase; ACE, angiotensin-converting enzyme; GABA (A/B), γ-aminobutyric acid; NGF, nerve growth factor; NI, not investigated; NMDA, *N*-methyl-D-aspartic acid. The appropriate plant part, as recommended in Ayurveda, was extracted with methanol by room temperature percolation. For biological screening, the methanol-free extract was taken up in aqueous DMSO to get 5 µg of the material/mL.

Learning, memory, and cognitive disorders. This area of research was selected for three reasons: *a*) there is a paucity of modern drugs/agents facilitating acquisition, retention, and retrieval of information and knowledge; *b*) with the increasing number of elderly people in the world population, the need for drugs to treat cognitive disorders, such as senile dementia and Alzheimer disease, have acquired special urgency; and *c*) Ayurveda claims that several plants, the so-called "medhya" plants, possess such activities.

The past two decades have seen tremendous advances in the area of brain physiology, learning, memory, and various brain disorders, and a host of mechanisms at molecular level have been delineated (*104–106*). Synapses—the junctions of nerve cells representing the basic interactive unit of neuronal circuits—constitute the fundamental systemic relationship within the brain. Understanding how this interactive multitude of neuronal circuitry is established initially, and refined continuously throughout life, is fundamental to understanding the molecular basis of learning and memory. At present, an impressive array of chemical entities affecting synapse formation, neuronal differentiation, neurotransmission, nerve growth and repair, and several other functions are recognized. Approximately 50 neurotransmitters belonging to diverse chemical groups have been identified in the brain (*107*). Receptors, which are activated by these chemicals, assume special importance in the present context. Specifically, *N*-methyl-D-aspartic acid (NMDA) and γ-aminobutyric acid (GABA) receptors have been implicated in learning and memory (*108–111*). It has been further postulated that $GABA_B$ antagonists may enhance memory (*108*), whereas the NMDA receptor has the ability to mediate synaptic plasticity (*111*). Acetylcholine, the first neurotransmitter to be characterized, has a very significant presence in the brain; recently, Winkler et al. (*112*) determined that acetylcholine is essential for learning and memory. Acetylcholine has been a special target for investigations for almost two decades because its deficit, among other factors, has been held responsible for senile dementia and other degenerative cognitive disorders, including Alzheimer disease (*113–116*). Approximately 5% of the neurons in the hippocampus (the part of the brain central to learning, memory, and emotions) disappears with each decade after 50 years of age, and the brain tries to compensate for this by further growth of the neurites (neuron axon and dendrites) (*117*), which are vital for normal functioning of the brain. Thus, nerve growth factor has an important role to play. Several reports have suggested that angiotensin-converting enzyme inhibitors (e.g., captopril) may indirectly lead to improved cognitive performance (*116*). There are several other factors [e.g., gonadal steroid receptors (*118,119*)], that have a bearing on learning and memory, but they are not relevant to the current work.

The knowledge about neurotransmitters, enzymes, growth factors relevant to memory and learning, and cognitive disorders is already being used for the discovery and development of suitable therapeutic agents (*120,121*). Major emphasis has been on acetylcholine. Because the number of acetylcholine receptors declines with advancing age, inhibitors of acetylcholine esterase (AChE), which terminates the action of acetylcholine, have been special targets for development.

We studied some of the Ayurvedic plants reputed to be memory enhancers (medhya) and antiaging drugs (Vayahsthapana) by standard receptor binding and enzyme inhibition techniques (Table 5), with the specific aim of identifying any leads based on the above considerations. It was gratifying to see several positive results. Shankhapushpi (leaf) is one of the prime medhya plants of Ayurveda; it may be useful for neural regeneration and synaptic plasticity. Jataamansi (rhizome) appears to be an excellent candidate for a potential inhibitor of AChE. Haritaki (fruit) is highly prized in Ayurveda for antiaging; its extract has displayed several activities. Ashwagandha (root) is another important antiaging plant. We have investigated this plant in some detail because its extract showed high affinity for both $GABA_A$ and $GABA_B$ receptors. Receptor-binding assay-guided fractionation of the crude methanol extract resulted in a butanol fraction with retention of $GABA_B$ receptor activity [concentration that inhibits 50% (IC_{50}) ~ 47 μg/mL] and an aqueous fraction that retained both $GABA_A$ (IC_{50} ~ 0.37 μg/mL) and $GABA_B$ (IC_{50} ~ 15.8 μg/mL) affinities.

Gastrointestinal disorders, satiety and feeding behavior. Cholecystokinin (CCK) is a polypeptide hormone, widely distributed in the gastrointestinal tract and nervous system (both peripheral and central); it plays a major role in the digestive process. CCK also occurs in the brain, where it acts as a neurotransmitter and neuromodulator. CCK exists as several different molecular species: CCK-58, CCK-39, CCK-33, CCK-8, and CCK-4. The octapeptide CCK-8, for example, predominates in the brain. Also, there are at least two types of CCK receptors (*122–124*).

Over the past 10–15 years, there has been much activity in the development of potent and selective CCK agonists and antagonists because these agents may lead to novel therapy for the treatment of disorders such as gastrointestinal disturbances, pancreatitis, gastric and pancreatic carcinomas, obesity, and cognition dysfunction, in which CCK has been implicated. Several such molecules are under active development (*124*). There are also satiety agents, fashioned after CCK, which may fight obesity (*125*).

It seemed worthwhile to evaluate the three components of Triphala (three fruits), an Ayurvedic remedy for treating various gastrointestinal disorders. The three fruits are products of *Terminalia chebula* (Sanskrit: haritaki), *Terminalia bellerica* (bibhitaka), and *Emblica officinalis* (aamalaki); haritaki has also been recommended in Ayurveda for treatment of obesity. The methanol-extracted material from the three fruits was evaluated *in vitro* by radioligand binding assays (Table 6) (*126*). As is evident from these data, the three extracts showed good affinity for the CCK receptor, thus, offering good opportunity for the isolation and evaluation of new and possibly clinically useful ligands. My laboratory investigated the extract from *T. bellerica* in some detail and isolated several pure compounds, one of which (code name B_3EA-10; melting point 190–192°C) showed high affinity (IC_{50} ~ 1.8 μg/ mL).

Hair growth promoting activity. A number of plants have been recommended in the Ayurvedic system for promoting the growth of head hair, as distinct from the treatment of alopecia, male pattern baldness. Because the research division of Hindustan Lever (Mumbai, India) had devised a system for screening plant extracts that may promote

Table 6. Cholecystokinin (peripheral) receptor binding assay of triphala components

Plant	Percent inhibition
Terminalia chebula	96
Terminalia bellerica	91
Emblica officinalis	76

The dried kernel-free fruits were extracted with methanol by room temperature percolation. For biological screening, the methanol-free extract was taken up in aqueous DMSO to get 5 μg of the material/mL.

Table 7. Angiogenesis assay (chorioallantoic membrane assay).

Botanical	Sanskrit	Plant part	Results
Embellica officinalis	Amalaki	Fruit	–
Hedychium spicatum	Shati	Root	New growth
Hemidesmus indicus	Saariva	Root	Bundling and new growth
Nardostachys jatamaansi	Jataamaansi	Root	New growth
Nigella sativa	Krishna jeeraka	Seed	–
Saussurea lappa	Kushth	Root	Bundling and new growth

hair growth, I sent them extracts of plants selected on the basis of claims of hair growth in the traditional medicine literature. The test system is based on the premise that transport of nourishment to the hair root, the site of biochemical activity, would be facilitated by strengthening the hair root system. For this they used the chicken chorioallantoic membrane assay, a model for angiogenesis (neovascularization). Normally, angiogenesis is unimportant except during growth and wound healing, and researchers have been seeking inhibitors of angiogenesis in search of anticancer compounds (*127*). However, my interest was to see if any of the traditional plants promote neovascularization because this would aid blood supply to the hair papilla. Table 7 summarizes these investigations; several positive results are evident.

Conclusion

The materia medica of Ayurveda, and other similar repositories of knowledge from other cultures, represent a valuable resource for development of not only medicinal preparations but also nutraceuticals and cosmaceuticals according to modern-day requirements. However, these claims must be critically evaluated in terms of modern scientific parameters. When such a project is envisaged, some prerequisites must be met. It is important to carefully correlate the disease description in the ancient literature with the modern etiology and clinical picture to ensure correct correspondence. In the Ayurvedic literature, there was much stress on the collection of plant material during a particular season, from a particular locale, and at a certain time of day. It is now well established that the concentration and profile of secondary metabolites in a plant depend on environmental, nutritional, and and photoperiodicity factors. Thus, the correct type of plant material is essential. Because traditional plant preparations have significant historical background, it may be ethical to clinically evaluate these first and then collect modern toxicologic data. For herbal preparations, it may not be essential to pinpoint the active principle(s), but it is desirable to have this information. In any case, important classes of compounds essential for biologic activity must be delineated. All of this knowledge will be essential for proper standardization of a product. If a product is too complex, it must be standardized in terms of biologic activity parameters. This will require much research effort.

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